DATE: 02/14/2002

PATENT APPLICATION: US/09/313,942

TIME: 15:49:04

Input Set : A:\REG203.txt

Output Set: N:\CRF3\02142002\I313942.raw

ENTERED

```
4 <110> APPLICANT: REGENERON PHARMACEUTICALS, INC.
      6 <120> TITLE OF INVENTION: RECEPTOR BASED ANTAGONISTS, AND METHODS OF MAKING
              AND USING
      9 <130> FILE REFERENCE: REG 203-A
C--> 11 <140> CURRENT APPLICATION NUMBER: US/09/313,942
     12 <141> CURRENT FILING DATE: 1999-05-19
     14 <150> PRIOR APPLICATION NUMBER: 09/313,942
     15 <151> PRIOR FILING DATE: 1999-05-19
     17 <150> PRIOR APPLICATION NUMBER: 60/101,858
     18 <151> PRIOR FILING DATE: 1998-09-25
     20 <160> NUMBER OF SEQ ID NOS: 32
     22 <170> SOFTWARE: FastSEQ for Windows Version 3.0
     24 <210> SEQ ID NO: 1
     25 <211> LENGTH: 6
     26 <212> TYPE: PRT
     27 <213> ORGANISM: Artificial Sequence
     29 <220> FEATURE:
     30 <223> OTHER INFORMATION: Tag sequence
     32 <400> SEQUENCE: 1
     33 His His His His His
     34 1
     36 <210> SEQ ID NO: 2
     37 <211> LENGTH: 16
     38 <212> TYPE: PRT
     39 <213> ORGANISM: Artificial Sequence
     41 <220> FEATURE:
     42 <223> OTHER INFORMATION: peptide derived from region near C-terminus of
              gp130
     43
     45 <400> SEQUENCE: 2
     46 Cys Gly Thr Glu Gly Gln Val Glu Arg Phe Glu Thr Val Gly Met Glu
                                             10
     47
     49 <210> SEQ ID NO: 3
     50 <211> LENGTH: 16
     51 <212> TYPE: DNA
     52 <213> ORGANISM: Artificial Sequence
     54 <220> FEATURE:
     55 <223> OTHER INFORMATION: Kozak sequence
     57 <400> SEQUENCE: 3
                                                                                16
     58 cgccgccacc atggtg
     60 <210> SEQ ID NO: 4
     61 <211> LENGTH: 10
     62 <212> TYPE: PRT
     63 <213> ORGANISM: Artificial Sequence
                                           OK to Enter
```

IF I III

DATE: 02/14/2002

TIME: 15:49:04

```
Input Set : A:\REG203:tat
                Output Set: N:\CRF3\02142002\I313942.raw
65 <220> FEATURE:
66 <223> OTHER INFORMATION: J peptide
68 <400> SEQUENCE: 4
69 Gly Gln Gly Thr Leu Val Thr Val Ser Ser
70
     1
                     5
                                        10
72 <210> SEQ ID NO: 5
73 <211> LENGTH: 11
74 <212> TYPE: PRT
75 <213> ORGANISM: Artificial Sequence
77 <220> FEATURE:
78 <223> OTHER INFORMATION: J peptide
80 <400> SEQUENCE: 5.
   Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
82
    1
                                        10
84 <210> SEQ ID NO: 6
85 <211> LENGTH: 10
86 <212> TYPE: PRT
87 <213> ORGANISM: Artificial Sequence
89 <220> FEATURE:
90 <223> OTHER INFORMATION: linker sequence
92 <400> SEQUENCE: 6
93 Gly Ala Pro Ser Gly Gly Gly Arg Pro
94
    1
                     5
                                        10
96 <210> SEQ ID NO: 7
97 <211> LENGTH: 859
98 <212> TYPE: PRT
99 <213> ORGANISM: Homo sapiens
101 <400> SEQUENCE: 7
102 Met Val Thr Leu Gln Thr Trp Val Val Gln Ala Leu Phe Ile Phe Leu
103
                                         10
     Thr Thr Glu Ser Thr Gly Glu Leu Leu Asp Pro Cys Gly Tyr Ile Ser
105
    Pro Glu Ser Pro Val Val Gln Leu His Ser Asn Phe Thr Ala Val Cys
106
107
             35
     Val Leu Lys Glu Lys Cys Met Asp Tyr Phe His Val Asn Ala Asn Tyr
108
109
     Ile Val Trp Lys Thr Asn His Phe Thr Ile Pro Lys Glu Gln Tyr Thr
110
111
     Ile Ile Asn Arg Thr Ala Ser Ser Val Thr Phe Thr Asp Ile Ala Ser
112
113
                                         90
    Leu Asn Ile Gln Leu Thr Cys Asn Ile Leu Thr Phe Gly Gln Leu Glu
114
115
                                                         110
    Gln Asn Val Tyr Gly Ile Thr Ile Ile Ser Gly Leu Pro Pro Glu Lys
116
117
                                 120
             115
                                                    125
118
     Pro Lys Asn Leu Ser Cys Ile Val Asn Glu Gly Lys Lys Met Arg Cys
119
         130
                             135
    Glu Trp Asp Gly Gly Arg Glu Thr His Leu Glu Thr Asn Phe Thr Leu
120
```

Lys Ser Glu Trp Ala Thr His Lys Phe Ala Asp Cys Lys Ala Lys Arg

RAW SEQUENCE LISTING

PATENT APPLICATION:

US/09/313,942

145

121

122

DATE: 02/14/2002 TIME: 15:49:04

PATENT APPLICATION: US/09/313,942

Input Set : A:\REG203; txt
Output Set: N:\CRF3\02142002\1313942.raw

123					165					170		•			175	
124	Asp	Thr	Pro	Thr	Ser	Cys	Thr	Val	Asp	Tyr	Ser	Thr	Val	Tyr	Phe	Val
125				180					185			•		190		
126	Asn	Ile	Glu	Val	Trp	Val	Glu	Ala	Glu	Asn	Ala	Leu	Gly	Lys	Val	Thr
127			195					200					205			
128	Ser	Asp	His	Ile	Asn	Phe	Asp	Pro	Val	Tyr	Lys	Val	Lys	Pro	Asn	Pro
129		210		•			215					220				
130	Pro	His	Asn	Leu	Ser	Val	Ile	Asn	Ser	Glu	Glu	Leu	Ser	Ser	Ile	Leu
131	225					230					235					240
132	Lys	Leu	Thr	Trp	Thr	Asn	Pro	Ser	Ile	Lys	Ser	Val	Ile	Ile	Leu	Lys
133	_			_	245					250				•	255	
134	Tyr	Asn	Ile	Gln	Tyr	Arg	Thr	Lys	Asp	Ala	Ser	Thr	Trp	Ser	Gln	Ile
135				260	_			_	265				_	270		
136	Pro	Pro	Glu	Asp	Thr	Ala	Ser	Thr	Arg	Ser	Ser	Phe	Thr	Val	Gln	Asp
137	-		275	_				280	_				285			
138	Leu	Lys	Pro	Phe	Thr	Glu	Tyr	Val	Phe	Arg	Ile	Arg	Cys	Met	Lys	Glu
139		290				•	295					300	_			
140	Asp	Gly	Lys	Gly	Tyr	Trp	Ser	Asp	Trp	Ser	Glu	Glu-	Ala	Ser	Gly	Ile
141	305	-	•	_	-	310		_	_		315				_	320
142	Thr	Tyr	Glu	Asp	Arg	Pro	Ser	Lys	Ala	Pro	Ser	Phe	Trp	Tyr	Lys	Ile
143		-4			325			-	•	330			•	, -	335	
144	Asp	Pro	Ser	His		Gln	Gly	Tyr	Arg	Thr	Val	Gln	Leu	Val	Trp	Lys
145	•			340		•	-	•	345					350	_	_
146	Thr	Leu	Pro	Pro	Phe	Glu	Ala	Asn	Gly	Lys	Ile	Leu	Asp	Tyr	Glu	Val
147			355					360	_	-			365	-	•	
148	Thr	Leu		Arg	Trp	Lys	Ser	His	Leu	Gln	Asn	Tyr	Thr	Val	Asn	Ala
149		370	٠		•	-	375					380				
150	Thr	Lys	Leu	Thr	Val	Asn	Leu	Thr	Asn	Asp	Arg	Tyr	Leu	Ala	Thr	Leu
151	385	•				390					395	-				400
152	Thr	Val	Arg	Asn	Leu	Val	Gly	Lys	Ser	Asp	Ala	Ala	Val	Leu	Thr	Ile
153			•		405		-	•		410					415	
154	Pro	Ala	Cys	Asp	Phe	Gln	Ala	Thr	His	Pro	Val	Met	Asp	Leu	Lys	Ala
155			_	420		,			425					430		
156	Phe	Pro	Lys	Asp	Asn	Met	Leu	Trp	Val	Glu	Trp	Thr	Thr	Pro	Arg	Glu
157			435	_			,	440					445			
158	Ser	Val	Lys	Lys	Tyr	Ile	Leu	Glu	Trp	Сув	Val	Leu	Ser	Asp	Lys	Ala
159		450	•	_	-		455		_	_		460		•	_	
160	Pro	Cys	Ile	Thr	Asp	Trp	Gln	Gln	Glu	Asp	Gly	Thr	Val	His	Arg	Thr
161	465	•			•	470	•			,	475					480
162	Tyr	Leu	Arg	Gly	Asn	Leu	Ala	Glu	Ser	Lys	Cys	Tyr	Leu	Ile	Thr	Val
163	•			•	485					490	_	•			495	
164	Thr	Pro	Val	Tyr	Ala	Asp	Gly	Pro	Gly	Ser	Pro	Glu	Ser	Ile	Lys	Ala
165.	_ 		_	500		-	•		505					510	. –	
166	Tyr	Leu	Lys		Ala	Pro	Pro	Ser	Lys	Gly	Pro	Thr	Val	Arg	Thr	Lys
167			515			-		520	-	-			525	•		_
168	Lvs	Val	-	Lys	Asn	Glu	Ala	Val	Leu	Glu	Trp	Asp	Gln	Leu	Pro	Val
169	-4 -	530	- - 4	- 4 -		,	535	-			•	540				
170	Agn		Gln	Agn	Glv	Phe		Ara	Asn	Tvr	Thr		Phe	Tvr	Ara	Thr
171	545	, -1			1	550		- 3	~- 	-1-	555				- 3	560
	- T - C		•													-

DATE: 02/14/2002 TIME: 15:49:04

PATENT APPLICATION: US/09/313,942

Input Set : A:\REG203,txt
Output Set: N:\CRF3\02142002\1313942.raw

172 173	Ile	Ile	Gly	Asn	Glu 565	Thr	Ala	Val	Asn	Val 570	Asp	Ser	Ser	His	Thr 575	Glu
174 175	Tyr	Thr	Leu	Ser 580	_	Leu	Thr	Ser	Asp 585		Leu	Tyr	Met	Val 590		Met
176 177	Ala	Ala	Tyr 595		Asp	Glu	Gly	Gly 600		Asp	Gly	Pro	Glu 605		Thr	Phe
178 179	Thr	Thr 610	Pro	Lys	Phe	Ala	Gln 615		Glu	Ile	Glu	Ser 620		Glu	Pro	Lys
180			Asp	Lys	Thr	His 630		Cys	Pro	Pro	Cys 635		Ala	Pro	Glu	Leu 640
181	625 Leu	Gly	Glý	Pro			Phe	Leu	Phe			Lys	Pro	Lys		
183 184	Leu	Met	Ile		645 Arg	Thr	Pro	Glu		650 Thr	Cys	Val	Val		655 Asp	Val
185 186	Ser	His	Glu	Asb	Pro	Glu	Val		665 Phe	Asn	Trp	Tyr		670 Asp	Gly	Val
187 188	Glu	Val	675 His	Asn	Ala	Lys	Thr	680 Lys	Pro	Arg	Glu	Glu	685 Glņ	Tyr	Asn	Ser
189 190	Thr	690 Tyr	Arg	Val	Val	Ser	695 Val	Leu	Thr	Val	Leu	700 His	Gln	Asp	Trp	Leu
191 ⁻ 192	705 Asn	Glv	Lys	Glu	TVr	710 Lvs	Cvs	Lvs	Val	Ser	715 Asn	Lvs	Ala	Leu	Pro	720 Ala
193		_	_		725					730					735	
194 195			Glu	740		•		_	745	_	_			750		_
196 197	٠.		Tyr 755				•	760	_	_		•	765	_		
198 199	Val	Ser 770	Leu	Thr	Cys	Leu	775	Lys	GLY	Phe	Tyr	780	Ser	Asp	Ile	Ala
200 201	Val 785	Glu	Trp	Glu	Ser	Asn 790	Gly	Gln	Pro	Glu	Asn 795	Asn	Tyr	Lys	Thr	Thr 800
202 203	Pro	Pro	Val	Leu	Asp 805	Ser	Asp	Gly	Ser	Phe 810	Phe	Leu	Tyr	Ser	Lys 815	Leu
204 205	Thr	Val	Asp	Lys 820	Ser	Arg	Trp	Gln	Gln 825	Gly	Asn	Val	Phe	Ser 830	Cys	Ser
206 207	Val		His 835		Ala	Leu	His	Asn 840	His	Tyr	Thr	Gln	Lys 845		Leu	Ser
208	Leu	Ser	Pro	Gly	Lys	His			His	His	His					
209 211	<210>	850 Sec) TD	NO ·	R		855	,					•			
	<211>	-	_	_							,					
	<212>										·					
					omo	sap	lens									•
	<213> ORGANISM: Homo sapiens <400> SEQUENCE: 8															
217			Ala			Сув	Ala	Leu	Leu	Ala	Ala	Leu	Leu	Ala	Ala	Pro
218	1				5	_				10					15	
219	Gly	Ala	Ala		Ala	Pro	Arg	Arg		Pro	Ala	Gln	Glu		Ala	Arg
220	- -			20	_	_	_		25	_		•	_	30	 .	_
221	Gly	Val	Leu	Thr	Ser	Leu	Pro	_	Asp	ser	Val	Thr		Thr	Cys	Pro
222			35					40					45			

PATENT APPLICATION: US/09/313,942

DATE: 02/14/2002 TIME: 15:49:04

Input Set: A:\REG203.txt
Output Set: N:\CRF3\02142002\1313942.raw

223 224	Gly	Val 50	Glu	Pro	Glu	Asp	Asn 55	Ala	Thr	Val	His	Trp 60	Val	Leu	Arg	Lys
225 226	Pro 65		Ala	Gly	Ser	His 70	Pro	Ser	Arg	Trp	Ala 75	Gly	Met	Gly	Arg	Arg 80
227	=	Leu	Leu	Arg	Ser 85		Gln	Leu	His	Asp 90	Ser	Gly	Asn	Tyr	Ser 95	Cys
229	Tyr	Arg	Ala	_	_	Pro	Ala	Gly	Thr 105		His	Leu	Leu	Val 110	_	Val
230 231	Pro	Pro	Glu	100 Glu	Pro	Gln	Leu	Ser		Phe	Arg	Lys	Ser		Leu	Ser
232			115					120	_		· •		125	_	-1	_,
233 234	Asn	Val 130	Val	Cys	Glu	Trp	G1y 135	Pro	Arg	ser	Thr	Pro 140	ser	Leu	Tnr	Thr
235	-	Ala	Val	Leu	Leu		Arg	Lys	Phe	Gln		Ser	Pro	Ala	Glu	
236	145	61 =	~1	Dwo	Ove	150		Ser	G1n	Glu.	155 Ser	Gln	Tara	Dhe	Sor	160
237 238	Pne	GIH	GT'n	PIO	165	GIII	TÄT	SET	GIII	170	per	GIII	пув	FIIC	175	Cys
239	Glņ	Leu	Ala	Val		Glu	Gly	Asp	Ser	Ser	Phe	Tyr	Ile	Val	Ser	Met
240				180			_		185	_ •	_	_		190		
241	Cys	Val		Ser	Ser	Val	Gly	Ser	Lys	Phe	Ser	Lys	Thr 205	Gln	Thr	Phe
242 243	Gln	Glv	195	Glv	Tle	T.e.ii	Gln	200 Pro	Asp	Pro	Pro	Ala		Ile	Thr	Val
244	9111	210	Cys	GLY	***	204	215					220				,
245	Thr		Val	Ala	Arg	Asņ		Arg	Trp	Leu	Ser	Val	Thr	Trp	Gln	Asp
246	225				_	230					235		_	_	•	240
247	Pro	His	Ser	Trp		Ser	Ser	Phe	Tyr		Leu	Arg	Phe	Glu		Arg
248	M	A	31 0	Gl v	245	Sar	T.v.a	Thr	Dhe	250	ሞከተ	ጥጕኮ	Met	Val	255	Asp
249 250	TAT	ALG	VIG	260	ALY	Der	nyo	1441	265	211,4	1		1100	270		p
251	Leu	Gln	His		Cys	Val	Ile	His	Asp	Ala.	Trp	Ser	Gly	Leu	Arg	His
252			275					280		_		_	285			
253	Val		Gln	Leu	Arg	Ala		Glu	Glu	Phe	Gly		Gly	Glu	Trp	Ser
254 255	C 1	290	Sor	Dro	Glu	Ala	295	Gly	Thr	Pro	Tro	300 Thr	·Ġln	Ser	Arg	Ser
255 256	Glu 305	TTP	261	PIO	GIU	310	Mec	0.13		110	315				••••	320
257		Pro	Ala	Glu	Asn	-	Val	Ser	Thr	Pro	Met	Gln	Ala	Leu	Thr	Thr
258					325				_	330				_	335	S
259	Asn	Lys	Asp	_	Asp	Asn	Ile	Leu		Arg	Asp	ser	Ala	Asn 350	Ala	Thr
260 261	gar	T.Ou	Bro	340	Gln	Agn	λla	Glv	345 Glu	Pro	T.vs	Ser	Cvs		T.vs	Thr
262	SET	Leu	355	Val	GIU	vob	nau	360	0.2.0		275		365		-70	+
263	His	Thr		Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser
264		370					375					380		•		
265		Phe	Leu	Phe	Pro		Lys	Pro	Lys	Asp		Leu	Met	Ile	Ser	Arg
266	385	D=-	63	We 1	mh~	390	Va 1	v=1	V _P 1	Nen	395 Val	Ser	pio	Gla	Agn	400 Pro
267 268	Thr	PIO	GTA	AGT	405	Cys	AGT	AGT	AGT	410	147	AGT	440		415	
269	Glu	Val	Lvs	Phe	-	Tro	Tvr	Val	Asp		Val	Glu	Val	His		Ala
270				420					425					430		
271	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val

VERIFICATION SUMMARY

PATENT APPLICATION: US/09/313,942

DATE: 02/14/2002 TIME: 15:49:05

Input Set : A:\REG203.txt
Output Set: N:\CRF3\02142002\1313942.raw

L:11 M:270 C: Current Application Number differs, Replaced Current Application Number